

WHAT IS CLAIMED IS:

1. An isolated polypeptide comprising at least 10 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

5 2. The polypeptide of claim 1, comprising at least 15 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

3. The polypeptide of claim 2, comprising at least 20 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

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4. The polypeptide of claim 3, comprising at least 25 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

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5. The polypeptide of claim 4, comprising at least 30 contiguous amino acids of SEQ ID NO: 2, 4, 5 or 6.

6. The polypeptide of claim 5, comprising at least 50 contiguous amino acids of SEQ ID NO: 2 or 4.

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7. The polypeptide of claim 6, comprising an amino acids sequence of SEQ ID NO: 2, 4, 5 or 6..

8. The polypeptide of claim 1, further comprising a leader sequence operatively coupled to the amino terminus of the polypeptide.

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9. The polypeptide of claim 8, wherein the leader signal sequence is a Kaposi fibroblast growth factor signal sequence, HIV-1 Tat (48-60), D-amino acid-substituted HIV-1 Tat (48-60), arginine-substituted HIV-1 Tat (48-60), Drosophila Antennapedia (43-58), or a polyarginine polypeptide having at least 6 to 8 arginines.

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10. An isolated polynucleotide comprising a nucleic acid encoding a RAIN polypeptide.

11. The polynucleotide of claim 10, wherein the nucleic acid sequence is as set forth in SEQ ID NO:1 or SEQ ID NO:2.

12. A method of treating a subject with bone loss comprising inhibiting osteoclast precursor cell fusion by administering a RAIN polypeptide in amount effective to modulate RANK signaling.

13. A method of treating a subject with bone loss comprising inhibiting osteoclast precursor cell fusion by administering an effective amount of an expression vector, wherein the expression vector comprises a polynucleotide encoding a RAIN polypeptide under the transcriptional control of a promoter.

14. The method of claim 13, wherein the promoter is a constitutive promoter.

15. The method of claim 13, wherein the promoter is an inducible promoter.

16. The method of claim 13, wherein the expression vector comprises a viral vector.

17. The method of claim 13, wherein said administration is repeated.

18. The method of claim 16, wherein the viral vector is selected from the group consisting of vaccinia virus, adenovirus, herpesvirus, retrovirus, cytomegalovirus, and adeno-associated virus.

19. The method of claim 13, wherein said expression vector is delivered endoscopically, intravenously, intraarterially, intramuscularly, intralesionally, percutaneously, or subcutaneously.

20. A method for inhibiting osteoclast precursor cell fusion comprising contacting an osteoclast precursor cell with an expression vector that expresses a RAIN polypeptide.
- 5 21. The method of claim 20, wherein the expression vector is a plasmid expression vector.
22. The method of claim 21, wherein the expression vector is a viral expression vector.
- 10 23. A method of identifying a modulator of a osteoclast precursor fusion comprising:
(i) providing a cell deficient in a RAIN polypeptide;
(ii) contacting the cell with a candidate substance; and
(iii) comparing osteoclast cell fusion observed when the candidate substance is not added, wherein an alteration in osteoclast cell fusion indicates that the
15 candidate substance is a modulator of a osteoclast cell fusion.
24. The method of claim 23, wherein the candidate substance is a second cell, a cancer cell, a multiple myeloma cell, a peptide, a peptide mimetic or a small molecule.
- 20 25. The method of claim 23, wherein the candidate substance is selected from a small molecule library.
26. The method of claim 23, wherein the candidate substance is a protein.
- 25 27. The method of claim 23, wherein the candidate substance is a RAIN analogue.
28. The method of claim 23, wherein the cell deficient in a RAIN polypeptide comprises an inactivated RAIN gene.
- 30 29. The method of claim 23, wherein the cell deficient in a RAIN polypeptide expresses an antisense RAIN nucleic acid.